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Zymeworks Announces Updated Single Agent Data for HER2-Targeted Bispecific Antibody ZW25 at European Society for Medical Oncology (ESMO) Congress

September 28, 2019

- *Single Agent Activity and Durable Disease Control Across Multiple Tumor Types*
- *Data Support the Initiation of a Registration-Enabling Phase 2 Trial Evaluating Single Agent ZW25 in Second-Line HER2-Expressing Biliary Tract Cancers*

BARCELONA, Spain--(BUSINESS WIRE)-- Zymeworks Inc. (NYSE/TSX: ZYME), a clinical-stage biopharmaceutical company developing multifunctional therapeutics, today announced updated data from the ongoing multi-center Phase 1 clinical trial evaluating ZW25 in patients with HER2-expressing solid tumors, including biliary tract cancer (BTC), colorectal cancer (CRC), gynecological cancers, and gastroesophageal adenocarcinoma (GEA), in a poster discussion presentation at the ESMO 2019 Congress, taking place September 27 - October 1 in Barcelona, Spain.

"The data presented today at ESMO confirm previous findings that ZW25 monotherapy can provide durable disease control in patients with a variety of HER2-expressing solid tumors that have progressed following standard of care therapies, including HER2-targeted agents," said Diana Hausman, M.D., Chief Medical Officer at Zymeworks. "Notably, the single agent objective response rate in biliary tract cancer is highly encouraging given the poor prognosis and limited treatment options for these patients. We are working closely with regulatory agencies to initiate a registration-enabling Phase 2 trial in second-line HER2-expressing biliary tract cancer with the goal of bringing ZW25 to patients as quickly as possible."

Based on the data from the ongoing Phase 1 study, Zymeworks has initiated a broad clinical development program for ZW25 in multiple HER2-expressing cancers. In addition to the Phase 2 BTC trial announced today, Zymeworks is continuing to evaluate ZW25 as a potential treatment for patients with other HER2-expressing cancers, including CRC and gynecological cancers ([Phase 1: NCT02892123](#)). For patients with HER2-expressing GEA, ZW25 is being developed as a first-line treatment in combination with standard of care chemotherapy ([Phase 2: NCT03929666](#)). Zymeworks also plans to initiate a Phase 2 study of ZW25 in combination with a CDK4/6 inhibitor and hormone therapy in third-line HER2-expressing, HR-positive breast cancer.

ZW25 Clinical Results Presented Today

The Safety, Efficacy and Biomarker Results of the HER2-Targeted Bispecific Antibody ZW25 in HER2-Expressing Solid Tumors (Abstract# 3575, Poster Discussion on Saturday, September 28 at 4:30 pm CEST)

Findings from this ongoing Phase 1 study of ZW25 in patients with HER2-expressing solid tumors were last presented at the 2018 EORTC-NCI-AACR Symposium. The updated results were presented today by Dr. Funda Meric-Bernstram, M.D., Clinical Investigator and Chair of the Department of Investigational Cancer Therapeutics at The University of Texas MD Anderson Cancer Center.

Data were reported from 58 patients diagnosed with HER2-expressing solid tumors other than breast cancer who received ZW25 at the recommended dose of either 10 mg/kg weekly or 20 mg/kg every other week. Patients had a median age of 61 years and received a median of four prior therapies. Thirty-two (55%) patients received prior HER2-targeted therapies including 87% of GEA patients. Of all patients, 23 were diagnosed with GEA, 13 with CRC, nine with BTC, and 13 with other HER2-expressing cancers, including endometrial, ovarian, pancreatic, and salivary gland.

At the time of data cut-off, 46 of 58 patients were response evaluable. Overall, the majority of patients experienced a decrease in their target lesions with a disease control rate of 72%, comprising 16 (35%) patients with partial responses and 17 (37%) with stable disease. The objective response rate in the six evaluable biliary tract cancer patients was 67%, with the majority of patients experiencing disease control greater than six months. In the 11 CRC and 19 GEA patients, the objective response rates were 36% and 32%, respectively. The overall median progression-free survival was 5.2 months, with 27 (47%) of the 58 total patients still on study at the time of data cut-off.

Among all patients, ZW25 was well tolerated as an outpatient therapy. The most common adverse events were diarrhea, infusion-related reaction, and nausea. All treatment-related adverse events occurring in 10% or more of patients were Grade 1 or 2.

About the Phase 1 Clinical Trial

Zymeworks' Phase 1 study has three parts. From part one of the study (the dose-escalation phase), the recommended single-agent dose was determined to be 20 mg/kg once every two weeks or 10 mg/kg weekly. In the second part of the study (the cohort expansion phase), additional patients are being enrolled to further assess ZW25's single-agent tolerability and anti-tumor activity against a variety of cancer types in different settings. The third part of the study (the combination phase) is underway and evaluating ZW25 in combination with selected chemotherapy agents in gastroesophageal and breast cancer patients with HER2 high or lower HER2 expression levels.

About ZW25

ZW25 is being evaluated in Phase 1 and Phase 2 clinical trials across North America and South Korea. It is a bispecific antibody, based on Zymeworks' Azymetric™ platform, that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. This unique design results in multiple mechanisms of action including dual HER2 signal blockade, increased binding and removal of HER2 protein from the cell surface, and potent effector function leading to encouraging anti-tumor activity in patients. Zymeworks is developing ZW25 as a HER2-targeted treatment option for patients with any solid tumor that expresses HER2. The FDA has granted Fast Track designation to ZW25 for first-line gastroesophageal adenocarcinoma in combination with standard of care chemotherapy and Orphan Drug designation to ZW25 for the treatment of both gastric and ovarian cancers.

About Zymeworks Inc.

Zymeworks is a clinical-stage biopharmaceutical company dedicated to the development of next-generation multifunctional biotherapeutics. Zymeworks' suite of therapeutic platforms and its fully integrated drug development engine enable precise engineering of highly differentiated product candidates. Zymeworks' lead clinical candidate, ZW25, is a novel Azymetric™ bispecific antibody currently in Phase 2 clinical development. Zymeworks' second clinical candidate, ZW49, is a bispecific antibody-drug conjugate currently in Phase 1 clinical development and combines the unique design and antibody framework of ZW25 with Zymeworks' proprietary ZymeLink™ cytotoxic payload. Zymeworks is also advancing a deep preclinical pipeline in immuno-oncology and other therapeutic areas. In addition, its therapeutic platforms are being leveraged through strategic partnerships with nine biopharmaceutical companies. For more information, visit www.zymeworks.com.

Cautionary Note Regarding Zymeworks' Forward Looking Statements

This press release includes "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and "forward-looking information" within the meaning of Canadian securities laws, or collectively, forward-looking statements. Forward-looking statements in this news release include statements that relate to ZW25 and its potential as an anti-cancer treatment, Zymeworks' clinical plans and future results, Zymeworks' technology platform, and other information that is not historical information. When used herein, words such as "believe", "may", "plan", and similar expressions are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon Zymeworks' current expectations and various assumptions. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation, market conditions and the factors described under "Risk Factors" in Zymeworks' Quarterly Report on Form 10-Q for the three month period ended June 30, 2019 (a copy of which may be obtained at www.sec.gov and www.sedar.com). Consequently, forward-looking statements should be regarded solely as Zymeworks' current plans, estimates and beliefs. You should not place undue reliance on forward-looking statements. Zymeworks cannot guarantee future results, events, levels of activity, performance, or achievements. Zymeworks does not undertake and specifically declines any obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances, or to reflect the occurrences of unanticipated events, except as may be required by law.



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